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ARTICLE

Acute chorea: case series from the emergency room of a Brazilian tertiary-level center

Coreia aguda: série de casos de pronto atendimento de um centro terciário brasileiro

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ABSTRACT

Background: Chorea is a movement disorder characterized by random, brief and migratory involuntary muscle contractions. It is defined as acute when present within hours to days. Three main causes for this scenario have emerged as most likely: vascular, toxic-metabolic and inflammatory. **Objectives:** To identify the prevalence of the main etiologies and major clinical findings of acute chorea in the emergency room of a tertiary-level referral center; and to suggest an approach for guiding the diagnostic workup and clinical management. **Methods:** We retrospectively reviewed the clinical aspects and neuroimaging data of 10 patients presenting with acute chorea at the neurological emergency room of our hospital from 2015 to 2019. **Results:** Stroke was the most common etiology (50% of the cases). All of them were ischemic. It was noteworthy that only one case demonstrated the classical ischemic topographic lesion at the contralateral subthalamic nuclei. Regarding nonvascular etiologies, nonketotic hyperglycemia was the major cause, followed by drug-related chorea. One patient showed inflammatory etiology, which was probably Sydenham chorea reactivation. **Conclusion:** Acute chorea is an uncommon and challenging problem at the emergency room, often associated with potentially treatable causes. We suggest that use of the acronym DANCE (Diagnosis of chorea, Acute stroke protocol, Normal glucose levels, Check neuroimaging, Exposure to drugs) could form a potential initial approach in the evaluation, in order to emphasize causes that require prompt proper management (e.g. thrombolysis).

Keywords: Chorea; Dyskinesia; Stroke; Emergencies; Movement Disorders.

RESUMO

Introdução: Coreia é um distúrbio do movimento caracterizado por contrações musculares caóticas, migratórias, aleatórias e involuntárias. Usualmente, define-se como coreia aguda quando presente dentro de horas a dias. Neste cenário, três causas emergem como as mais comuns: vascular, tóxico-metabólica e inflamatória. **Objetivos:** O objetivo deste estudo foi identificar a prevalência das principais etiologias e os principais achados clínicos de coreia aguda na sala de emergência de um centro de referência terciário, a fim de sugerir uma abordagem para orientar a investigação diagnóstica e o manejo na emergência. **Métodos:** Revisamos retrospectivamente os dados clínicos e de neuroimagem, de 2015 a 2019, de 10 pacientes com coreia aguda na sala de emergência neurológica de um hospital terciário. **Resultados:** A etiologia mais comum foi o acidente vascular cerebral (AVC) (50% dos casos). Todos os AVCs foram isquêmicos e apenas um se apresentou como isquemia clássica do núcleo subtalâmico contralateral. Em relação às causas não vasculares, a hiperglicemia não cetótica demonstrou ser a principal, seguida pela coreia relacionada a medicamentos. Um paciente apresentou etiologia inflamatória, por provável reativação da coreia de Sydenham. **Conclusão:** A coreia aguda é um problema incomum e desafiador na sala de emergência, muitas vezes associado a causas potencialmente tratáveis. Nós sugerimos o acrônimo DANCE (*Diagnosis of chorea*, *Acute stroke protocol*, *Normal glucose levels*, *Check neuroimaging*, *Exposure to drugs*) para auxiliar na abordagem como primeiro passo na sala de emergência, a fim de enfatizar causas que requerem tratamento imediato e adequado (por exemplo, trombólise).

Palavras-chave: Coreia; Discinesias; Acidente Vascular Cerebral; Emergências; Transtornos dos Movimentos.

INTRODUCTION

Chorea is derived from the Greek word *choros*, meaning dance. It is a hyperkinetic movement disorder characterized by a continuous flow of random, brief and migratory involuntary muscle contractions. In the diagnostic workup of chorea, at least ask four questions should be asked: 1) What was the patient's age at onset? 2) What was the time course of chorea? 3) Was the patient exposed to drugs capable of inducing chorea? 4) Is there a positive family history for chorea?[1]

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According to the temporal pattern, chorea is defined as acute when present within hours to days. Unlike chronic chorea, in which heredodegenerative causes such as Huntington's disease stand out, three main nosologies have major roles in acute chorea: vascular, metabolic and inflammatory[2,3].

In the context of acute or subacute chorea, hemiballism-hemichorea is usually the most common presentation. Ballism is a term derived from the Greek word *ballismus*, which means "jumping about or dancing". This is generally considered to be a very severe variant of chorea characterized by violent, large-amplitude flinging movements involving proximal extremities on one side of the body. Due to its often-related acute onset, this presentation is the one most frequently seen in the emergency room[4,5]. Chorea or ballism are usually displayed in the same patient during the course of the disease; hemiballism is more prominent earlier, and lower-amplitude hemichorea emerges as the disorder evolves. Commonly, the terms are used interchangeably.

Abnormal movements develop as complications in 1–4% of all patients after stroke[6]. Although hemichorea is considered to be a rare complication reported in less than 1% of cases, with or without hemiballism, it is the most frequent hyperkinetic post-stroke movement disorder, followed by dystonia. In addition, hemichorea-hemiballism may be part of or even the only sign of acute presentation of chorea[6]. On the other hand, a previous case series on sporadic chorea in adults showed that stroke is the main cause of acute chorea (approximately 50%)[7].

Metabolic nosology often appears as the second main etiology, in up to 30% of cases[1,3]. Drugs, hyperglycemia, hyponatremia and hypoxemia have all been listed as potential causes. The possibly remaining etiologies are usually inflammatory, whether autoimmune or infectious (e.g. Sydenham or HIV-AIDS). Regarding case series of children with acute chorea, up to 95% present Sydenham chorea, such that inflammatory etiology is the most frequent cause in this specific population[1]. Other immunological etiologies resulting in chorea include systemic lupus erythematosus, primary antiphospholipid antibody syndrome, vasculitis and paraneoplastic syndromes.

Considering that acute chorea or hemiballism-hemichorea syndromes are uncommon entities that are found in the context of neurological emergencies, we conducted a retrospective study to investigate acute chorea cases evaluated over the past four years.

Regarding vascular causes, we described the vascular regions more commonly affected in cases of acute chorea. Concerning metabolic causes, we investigated which were the major underlying etiologies. From this, we put forward suggestions regarding the findings from clinical features that potentially would be capable of distinguishing between vascular and nonvascular (metabolic or inflammatory) etiologies, in order to guide approaches towards acute chorea syndromes and their management.

Hence, the main purpose of this study was to investigate which were the main etiologies and clinical features of acute chorea in the emergency department of a tertiary-level center. Additionally, we suggested an approach for optimizing the diagnostic workup and for the initial management of this uncommon condition in the emergency room.

METHODS

This was a retrospective observational study. We reviewed the electronic medical records of patients seen at the neurological emergency room of Hospital das Clínicas, University of São Paulo School of Medicine, from 2015 to 2019. We searched for the term "chorea" in summarized patient data. When records were found, we accessed the full medical record of each patient from the time of the emergency room admission. A total of 10 patients were included in the definition of acute chorea or hemiballism-hemichorea, based on clinical examination and according to the medical records. The data were then grouped into three main causes: vascular, toxic-metabolic and inflammatory.

In each case, we characterized the age at onset, gender, body distribution (hemichorea versus generalized chorea), duration of chorea at the time of hospital admission, neuroimaging characteristics and final etiology registered in the medical records. For acute chorea related to stroke, we also characterized the vascular regions.

All the analyses were performed using the Statistical Package for the Social Sciences software, version 21.0 (SPSS, IBM Statistics, Chicago, IL, USA). Categorical variables were expressed as absolute and relative frequencies and compared using Pearson's chi-square in univariate analyses. All tests were two-tailed. Statistical significance for final values was taken to be $p<0.05$.

RESULTS

In our series, data from 10 patients presenting with acute chorea in the emergency room were retrospectively evaluated. The investigations performed and described in the medical records were generally based on neuroimaging and laboratory tests. The patients' median age was 59 (± 18.38) years. The majority were female (70%) and the median duration of symptoms was six (±5.63) days. Regarding the etiology of the 10 patients with acute chorea, five cases (50%) presented vascular etiology, four cases (40%) had a metabolic cause and one case (10%) had an inflammatory cause (Table 1).

We compared age at onset, body distribution and median duration of symptoms in two groups: vascular and nonvascular causes. There were no statistical differences regarding age at onset, in a direct comparison between vascular and nonvascular causes (median age 59±21.34 vs 58±14.4 years). All vascular causes presented as hemichorea, whereas the most common body distribution in nonvascular etiologies was generalized (60%).

To compare the etiologies concerning presentation timing, we divided the acute chorea sample into two groups: from the beginning until 24 hours and more than 24 hours. Interestingly, the group with presentation of less than 24 hours was statistically related to the vascular etiology (p=0.04). It was noteworthy that the median duration of symptoms for vascular causes was 17 (±63.12) hours, in contrast to 14 (±3.97) days for nonvascular causes.

Considering the vascular-related cases, all of these five patients had asymmetrical presentation and ischemic strokes. Only one patient in this group (case 2 in Table 1) showed ischemia in the contralateral subthalamic nuclei (which is classically associated with hemichorea-hemiballism). Other regions of occurrence that were found included the caudate, insula and parietal lobe (Figure 1). Patient 5, a 59-year-old woman, developed hyperacute left hemichorea-hemiballism and was admitted within 60 minutes from the clinical onset, in our emergency department. Her head CT scan and blood glucose were normal. She underwent thrombolysis with intravenous alteplase, from which she evolved with partial improvement after 2 hours and complete resolution after 24 hours, without any other treatments. Brain MRI demonstrated acute right insular stroke. This remarkable example of a dramatic response emphasizes the importance of considering chorea in stroke protocols when there is an ictal onset, and of considering it to be a potentially treatable entity[8].

Regarding toxic-metabolic etiology, there were two cases of hemichorea-hemiballism secondary to decompensated diabetes with a nonketotic hyperglycemic state. In addition to high serum glucose levels, characteristic imaging signs of striatal hyperdensity on CT scan or hyperintensity on T1-weighted MRI in the basal ganglia aided the diagnosis. Both cases presented asymmetrical hemichorea syndromes and had benign evolution, with remission in which it took from days to weeks for the symptoms to improve after glucose control had been achieved.

Another two cases were defined as drug-induced. A 61-year-old patient with generalized chorea and encephalopathy, with laboratory results showing a lithium level of 3.17 mmol/L (therapeutic range 0.5–0.8 mmol/L), underwent hemodialysis and subsequently became more alert, and the chorea subsided. Patient 8, a 49-year-old male, developed generalized chorea after introduction of a selective serotonin reuptake inhibitor (SSRI), fluoxetine, at a standard dose. Further laboratory and imaging investigations were unremarkable and no other potential factor was identified. The medication was discontinued and chorea improved after SSRI withdrawal.

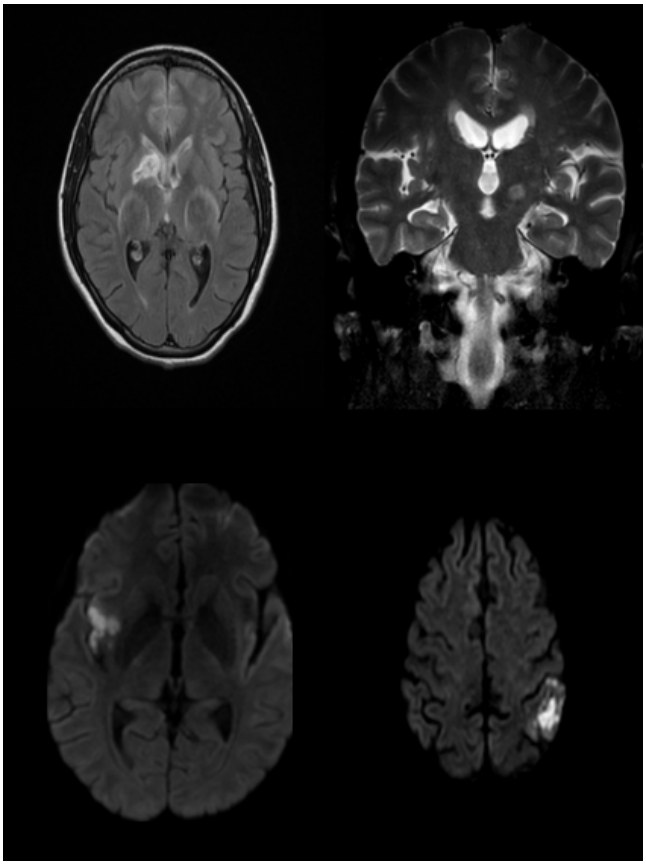

Figure 1. Vascular chorea: although classically described in the subthalamic nuclei, our cases showed ischemic lesions in other parts of the basal ganglia network: caudate nuclei, globus pallidus and parietal and insular cortex.

Table 1. Demography, body distribution, etiology, neuroimaging and duration of symptoms of 10 cases with acute chorea.

Case	Age	Gender	Distribution	Etiology	Neuroimaging	Duration of symptoms
1	20	F	Hemichorea	Vascular	Caudate ischemia	17 hours
2	59	M	Hemichorea	Vascular	Subthalamic nuclei ischemia	7 days
3	65	M	Hemichorea	Vascular	Parietal ischemia	1 day
4	86	F	Hemichorea	Vascular	Parietal ischemia	2 hours and 40 minutes
5	59	F	Hemichorea	Vascular	Insular ischemia	1 hour
6	58	F	Hemichorea	Metabolic (diabetes)	Basal ganglia hyperdensity	14 days
7	61	F	Generalized	Metabolic (lithium)	Normal	5 days
8	49	M	Generalized	Metabolic (SSRI)	Normal	7 days
9	69	F	Hemichorea	Metabolic (diabetes)	Basal ganglia hyperdensity	14 days
10	27	F	Generalized	Inflammatory (Sydenham)	Normal	14 days

One case in the sample had an inflammatory cause. This comprised probable reactivation of Sydenham chorea in a 27-year-old female patient. She presented involuntary movements days after a dental procedure, with phenomenology similar to what had been seen when she was previously diagnosed with Sydenham chorea in childhood. After ruling out other causes of chorea through her history, neuroimaging and laboratory testing, we considered that this case probably represented reactivation of Sydenham chorea.

Neuroimaging was useful in all vascular cases and in metabolic chorea associated with nonketotic hyperglycemia. There were no typical relevant abnormalities presented in neuroimaging, concerning drug-related and inflammatory causes (Sydenham reactivation), in contrast to the vascular etiologies and hyperglycemic states (brain MRI was performed on all our cases). The most useful laboratory tests in our sample were seen to be the serum glucose and drug serum levels (e.g. lithium).

DISCUSSION

In our case series, acute chorea was more commonly found in middle-aged adults, probably due to the main vascular etiology. Although our sample was of limited size, this finding is in line with a previous Italian case series in which 51 patients with acute chorea were described[7]. On the other hand, a previous Brazilian case series demonstrated a younger mean age[9].

Vascular etiology was the main cause of acute chorea in our patients. This result is consistent with two other previous case series[7,9]. Ischemic stroke occurred in all the vascular cases, as was seen in these previous studies, in which all the cases were due to ischemic stroke except for one in which acute chorea was developed after a left caudate hematoma[7].

Although occurrences of chorea are classically associated with subthalamic nuclei infarction, previous studies have shown that neuroimaging findings in other region are the rule and not the exception (Figure 1) [7,9]. Chorea should be recognized as caused by dysfunctional neuronal networks connecting the basal ganglia and motor cortical areas, and not due to a single lesion related to a specific brain topography (e.g. subthalamic nuclei). One possible network with a considerable role is the posterolateral putamen pathway, which was shown to be damaged in 90% of the patients in a hemichorea-hemiballismus case series with 29 patients[10]. The sites involved included the caudate nuclei, insular cortex and parietal lobe, regions that were also identified in our case series (Figure 1).

Toxic-metabolic causes were the second most frequent etiology. Nonketotic hyperglycemia was the main etiology in this group. Similar findings were reported in a previous case series[7,9]. It has been acknowledged that, although metabolic etiologies are often associated with diffuse brain lesions and generalized chorea, the distribution in nonketotic hyperglycemia is usually unilateral[1,11]. This distribution possibly makes nonketotic hyperglycemia the main differential diagnosis of vascular chorea. One reasonable previously mentioned explanation is that hyperglycemia leads to multifocal asymmetrical petechial hemorrhages of the basal ganglia, which is highlighted by the typical asymmetric hyperdense basal ganglia lesions in brain CT, which correlate with SWI-positive findings in brain MRI[1]. This imaging pattern was found in both our cases, thus aiding in the differential diagnosis, and is in contrast with a previous case series in which it was only seen in three out of six cases[12].

We did not find any cases of the following causes of metabolic chorea that have previously been described: acute intermittent porphyria, hypo/hypernatremia, hypocalcemia, hyperthyroidism, hypoparathyroidism or hepatic/renal failure.

Additionally, drug-related chorea cases presented as generalized chorea syndrome. Several centrally-acting drugs, such as as neuroleptics, metoclopramide, lithium, SSRI and cocaine, have previously been identified as possible causes of medication-induced chorea[7,13,14]. One previous case report describing lithium toxicity leading to sporadic chorea mentioned risk factors such as advanced age, use of concomitant medications and impaired kidney function[14]. Other less common substances that have been reported as causes of drug-induced chorea include carbon monoxide, manganese, mercury and organophosphate poisoning[1].

In our case series, only one case had an inflammatory cause, consisting of probable Sydenham chorea reactivation. We assume that the reason for this was that the most common inflammatory chorea, Sydenham chorea, is typically a pediatric disease and our service is an adult-only emergency department.

Furthermore, differently from the previous case series, we did not see any HIV-related chorea, which has been mentioned as the most common infectious cause[7]. One reasonable explanation for this could be the lower incidence of uncontrolled HIV-AIDS nowadays. It is worth mentioning that we also did not find any other causes of inflammatory chorea that have been described, such as chorea gravidarum, antiphospholipid antibody syndrome, postinfectious or post-vaccinal encephalitis. paraneoplastic chorea, neurosyphilis or viral encephalitis (mumps, measles and varicella), mainly due to our small sample. A longer period for an observational study would probably give rise to some of these etiologies.

Taking into account our findings, we developed the DANCE investigational acronym to suggest some first steps in the approach towards patients presenting with acute chorea in the emergency room. This is a mnemonic that represents the following: Diagnosis of chorea, Acute stroke protocol, Normal glucose levels, Check neuroimaging and Exposure to drugs (DANCE). Its aim is to enable identification of common etiologies that require urgent management, as shown in Table 2. We recommend that acute stroke protocol evaluation should be performed even in patients with diabetes and

Table 2. The DANCE approach. The five critical points in patients with acute chorea are the following: identification of a chorea syndrome; use of an acute stroke protocol; presence of normal serum glucose; checking of neuroimaging; and checking of exposure to drugs.

Diagnosis of chorea	Involuntary migratory, random, chaotic muscle contractions
Acute stroke protocol	Thrombolysis can be as adequate for acute hemichorea as it is for acute hemiparesis
Normal glucose protocol	Nonketotic hyperglycemia is a major cause of acute chorea
Check neuroimaging	Order brain imaging (consider MRI if CT is normal)
Exposure to drugs	Stop use of centrally-acting drugs as neuroleptics, lithium or SSRI

elevated serum glucose at admission, because these patients also present increased risk of stroke, and thrombolysis is a time-limited form of therapy. Brain MRI imaging is often able to help differentiate stroke and hyperglycemia as the cause of acute chorea.

As a retrospective case series, there were some limitations regarding collection of data from non-standardized medical reports. Two patients were excluded prior to the analyses due to incomplete descriptions of the etiology investigation. Furthermore, the low volume of data prevented us from obtained more robust statistical relevance. Nonetheless, we consider that one strength of our study was that it illustrates a case series of a rare movement disorder presentation in the emergency department. In addition, we proposed a diagnostic workup based on our clinical observations, within the acute context of generalized chorea or hemiballism-hemichorea syndromes. Therefore, considering the emerging developments regarding stroke protocols and neuroimaging, we are sure that a straightforward approach might help in making prompt diagnoses and in managing this potentially treatable entity .

Acute chorea is an uncommon problem in the emergency room that is associated with potentially treatable causes. The main etiology is vascular and, thus, it should be considered in stroke protocols aiming towards thrombolysis. The initial investigation also should focus on serum glucose levels, given that nonketotic hyperglycemic states are other frequent cause. Ascertaining the patient's drug history is paramount, in order to rule out centrally-acting drugs as an etiology relating to chorea (e.g. lithium). Neuroimaging can help in the differential diagnosis between stroke and nonketotic hyperglycemia. We proposed the DANCE approach (Table 2) to guide the diagnostic workup and to emphasize the first steps in evaluating patients with acute chorea, in order to focus on causes that require prompt management, such as thrombolysis, hemodialysis or intensive glucose control.

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